

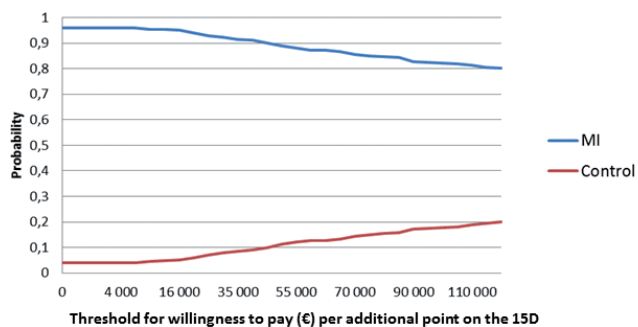


Fig. S1. Cost acceptability for incremental costs per quality-adjusted life years (QALY) for the motivational interviewing (MI) intervention compared with treatment-as-usual (TAU). Cost acceptability curve 6 months after climate heliotherapy (CHT).

Appendix S1

MATERIAL AND METHODS

Study design and participants

This economic evaluation was designed alongside a randomized controlled trial of 169 Norwegian patients participating in CHT. Patients were 20–70 years old with moderate to severe psoriasis (PASI >7 at application), were capable of answering questionnaires and communicating by telephone. Full inclusion and exclusion criteria are presented in the original clinical paper (11).

Ethical approval

Throughout the study, the principles outlined in the Declaration of Helsinki were followed (12). The study was approved by the research director and the Centre for Privacy and Information Security at Oslo University Hospital and also by the Regional Committee for Medical Research Ethics for Southern Norway (ID: 2011/1019) and registered at: <http://www.clinicaltrials.gov> (ID: NCT 01352780).

Climate therapy programme

CHT includes individualized sun exposure in increasing doses as the main treatment. Thus, the sun exposure is dependent on skin type and the current ultraviolet (UV) index. In addition, the programme emphasizes daily physical training, tailored education, group discussions and individual consultations and supervision by nurse and dermatologist. Hence, the 3 weeks of CHT programme consists of both sun treatment and patient education (Table SII¹).

Motivational interviewing

Motivational interviewing (MI) is defined as "a collaborative, conversation style for strengthening a person's own motivation and commitment to change" (10, 12). The MI counsellor focuses on assisting patients to identify their problems and also overcome ambivalence and resistance to behaviour change. Thus, MI is a method of engaging with patients to enable them to make their desired changes to personal health behaviours. A key goal is to increase the importance of change from the client's perspective. This is accomplished by for example using specific types of open-ended questions, selective reflections, summaries and reflective listening (10). For example, by estimating the importance of and their personal readiness for changing the desired behaviour, the patients may strengthen their determination to change and achieve increased self-efficacy.

Intervention

Both groups participated in CHT prior to the MI intervention and were randomized to the control or the intervention group after discharge, 1–2 days before returning to Norway. A more detailed description of the intervention is published elsewhere (11). Briefly, patients in the study group received 1 face-to-face mapping conversation (45–60 min) with the MI counsellor (main author) before returning home from Gran Canaria and 6 follow-up calls using the MI technique during the next 12 weeks. The follow-up calls discussed on 4 main self-management domains: diet, physical activity, stress management and psoriasis treatment, with psoriasis treatment as the only mandatory topic for each call. Patients could also choose other behaviour topics, perceived to be more important

to them; such as smoking cessation, weight reduction or alcohol abuse, or domains of life that caused stress or concern, such as demanding work situations, personality traits or traumatic life events. A bubble sheet for agenda mapping was used to identify a first focusing domain to pursue change (11).

In addition, participants received a personal workbook with some open questions for reflection about change and some visual MI tools and exercises. The duration of the calls was between 15 and 60 min. The mean (SD) conversation time was 32.5 (SD 12.7) min and each participant received a mean of 3.3 (SD 1.3) h of phone counselling. Participants allocated to the control and study groups all obtained psoriasis TAU (from a dermatologist or a general practitioner (GP)) according to the usual clinical practice after they returned to Norway.

Measures

Information about health outcomes and costs are collected from self-reported questionnaires, which were collected at baseline (at arrival for CHT), at 3 months, and at 6 months post-randomization (after 3 weeks of CHT). The baseline questionnaires covered resource use during the 3-month period prior to the baseline assessment.

Health outcomes

The health outcomes were measured in quality-adjusted life years (QALYs). QALY is a generic measure that includes both quantity (duration of time in a state of health) and health-related quality of life (HRQoL) generated by healthcare interventions (13). One year of perfect health equals 1 QALY. We used the 15D instrument, a generic, comprehensive, self-administered measure of HRQoL. It consists of 15 dimensions: mobility, vision, hearing, breathing, sleeping, eating, speech, elimination, usual activities, mental function, discomfort and symptoms, depression, distress vitality and sexual activity. Each dimension has 5 levels ranging from "no problems" to "extreme problems" (14). Based on the Finnish valuations, the single index (15D score) was calculated on a scale from zero (equivalent to being dead) to 1 (equivalent to full health, i.e. no problems on any dimension). The questionnaire is well validated and easy to use (14) (<http://www.15d-instrument.net>). The Cronbach's alpha was 0.81 for this study. A difference of 0.015 was recently stated as the minimum important change in 15D scores (15).

We also investigated the scenarios when QALYs were calculated from the Dermatological Life Quality Index (DLQI-N). DLQI is a well-validated, dermatology-specific, quality-of-life form (16). In this study, Cronbach's alpha was 0.90.

Cost

Information on healthcare utilization, medication, participants' costs and productivity loss was obtained through the 3-month and 6-month questionnaires. Information on cost per unit was collected from several sources (Table SII¹).

The different costs are analysed and presented in 3 different cost categories (Table SIII¹). Cost group 1 includes direct costs for primary and secondary healthcare services. Patients were asked to recall use of hospital services (i.e. outpatient and inpatient consultations, UV light treatment), medical specialists care (e.g. GP, dermatologist and rheumatologist), allied healthcare (e.g. physiotherapist and psychologist), as well as use of alternative medicine care (e.g. healer and acupuncture). Here we assessed the costs according to charge per treatment or Diagnosis-Related Group (DRG) codes for 2012. The DRG system classifies hospital services into groups that are medically related and homogeneous with regard to use of resources. DRG

is a way of describing the hospital's case-mix and depends on the patient's diagnosis, the procedures performed, complicating conditions, age, and discharge status. Each DRG is given a weight that reflects the treatment cost relative to an average patient. Thus, a more resource-intensive treatment will provide higher reimbursement than less resource-intensive treatment (17). In 2012, the cost for 1 DRG point was €5,112 referring to an average patient. Travel cost was added to consultations with specialists, psychologists and hospital visits. UVB treatment was estimated together with reported travel costs from the questionnaires. Appointments at a GP's office and with a physiotherapist, chiropractor, etc. were considered as zero travel costs, as these services are often received close to home.

Cost group 2 contains pharmaceuticals and use of prescribed psoriasis medication (systemic and topical). The impact on cost of "over-the-counter" (OTC) and self-care products that were skin care related was also expected to be relevant. To estimate the cost all concomitant medication registered by start and stop dates were added for each patient and period. The assessments also included volume of applied topical treatment and OTC moisturizing creams and emollients. Here we used the prices (in 2012) from a local pharmacy and The Norwegian Pharmaceutical Product Compendium. Regarding biological medicines we used DRG codes for 2012.

Cost group 3 covered cost for production loss for employed patients. Productivity loss is limited to work absenteeism and defined as productivity loss due to health-related absence from work (18). Changes in work status were recorded on the follow-up questionnaires. Patients who were students, unemployed, retired due to age, or on disability pension were excluded, as they were presumed to have no productivity losses. The human capital approach was used to estimate the costs of sick leave (19), estimated as the number of days each participant was absent from work due to psoriasis. This cost was estimated to be equal to average income and social costs. We used the median gross income in 2012 in Norway (NOK446,200=€59,732 per year) (Statistics Norway 2012, <http://www.ssb.no>) adjusted by 1.4 to account for social costs. For patients who were able to work part-time, this productivity cost was reduced in proportion to the time worked.

The cost of delivering the intervention is presented in Table SII¹.

Economic evaluation

We calculated QALYs by plotting HRQoL against time and applying the area under the curve approach using the trapezoidal method (20). This procedure generates a QALY gained for each patient over the 6-month period of the study. The 2 trial groups were then compared with generate the estimate of

mean differential QALY. The incremental cost-effectiveness ratio (ICER) was calculated as the mean difference in costs between the 2 groups divided by their difference in QALYs gained, defined by:

$$\text{ICER} = \frac{\text{Cost of intervention} - \text{Cost of TAU}}{\text{Health effect of MI intervention} - \text{Health effect TAU}} = \frac{\Delta C}{\Delta E}$$

Because a positive outcome is measured by a reduction in DLQI, we adjusted for this by including a negative sign in the definition of the ICER including DLQI. To avoid ambiguous interpretations of the ICER, we also report the findings by Net Monetary Benefit (NMB), defined by $\text{NMB} = \lambda * \Delta E - \Delta C$, where lambda (λ) is the threshold value for a health gain and is suggested to be €62,500. All else equal, one should adopt programmes with net monetary benefit that are greater than 0 (19). The 95% confidence interval (95% CI) around the mean cost per patient and the between-group differences in mean total costs were estimated with bootstrapping, repeating the analysis 1,000 times. Cost-effectiveness acceptability curves (CEACs) were estimated to consider the uncertainty surrounding the cost-effectiveness (in €) of the MI programme by plotting the probability that the MI intervention and TAU is cost-effective according to threshold values, i.e. the decision-maker's willingness to pay for an additional QALY (21, 22).

Statistical analysis

Normal distributed continuous data are indicated as mean value with standard deviation (SD). Non-normally distributed data are indicated as median value with the minimum and maximum values. To analyse differences between groups, we used independent sample *t*-tests with corresponding 95% confidence intervals and non-parametric analysis (Mann-Whitney *U* test) to compare, respectively, normally distributed and non-normally distributed continuous data. Two-sided $p < 0.05$ were regarded as significant.

SPSS version 21 was partially used for the analyses (SPSS Inc., Chicago, IL, USA). We used STATA to estimate uncertainty around the ICER using bootstrapping, generating 1000 replications of each ratio (replicated ICERs). Cost-effectiveness acceptability curves (CEAC) were calculated in Excel. In addition, we controlled for imbalance in baseline HRQoL in the estimation of mean differential QALYs by regression analysis, as recommended by Manca et al. (23). Missing values on cost items, healthcare utilization, psoriasis treatment and self-care products in the questionnaires were consequently set at zero. Costs were calculated in Norwegian kroner (NOK) and presented in Euros (€), using an exchange rate of €1=NOK7.47 (medium value in 2012). All costs and outcomes fell within a 6-month period, and therefore discounting was not appropriate.

Table SI. Aims and content of the Norwegian climate/heliotherapy programme in Gran Canaria

Aims

- Reduce disease severity
- Increase knowledge and insight about the disease, treatment and symptom management
- Increase awareness about how to reduce deteriorating risk factors, such as smoking, stress and overweight
- Discuss recent knowledge about psoriasis comorbidity, how to reduce risk profiles and motivate positive lifestyle changes

Content

- Examination by the dermatologist and nurse on 3 occasions (at arrival, after 1 week and after 3 weeks) and personalized follow-ups when needed
 - A combination of tailored sun treatment and salt-water bathing. Exposure according to skin type and current ultraviolet index
 - Physical activities: morning "workout" and voluntary participation in other physical activities, such as water aerobics, walking/running, swimming, muscular training and relaxation techniques
 - Interactive educational sessions conducted by a dermatologist, nurses and physiotherapist about psoriasis pathogenesis, manifestations, comorbidity, quality of life and treatment options and the importance of a healthy lifestyle focusing on physical activity, stress reduction and healthy eating.
 - Educational sessions: creams and ointments (2 h), sun treatment (1 h), nutrition (2 h), physical activity (1 h), education about psoriasis (2 h), comorbidity related to the disease (1 h), medical treatment (2 h) and research (1 h)
 - Group meetings (8–12 participants) focused on experiences of living with psoriasis, coping with stress, nutrition in daily life and self-management (1–3 h)
 - Voluntary smoking cessation course (4–6 h)
 - Interaction with others with similar health challenges in formal and informal settings
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Table SII. Unit costs of resources used

Cost categories	Unit	Valuation	Costs (€) ¹	Source
Prepare MI calls and write summary	Per patient	(10 min/call×6 calls: €31.9×1.4)	44.62	Norwegian Nursing Association
Mapping talk (total 60 min)	Per patient	60 min	44.62	Norwegian Nursing Association
3 days course to master MI techniques	Per patient	((7.5h×€31.9×3 days)×1.4)/86 patients	11.68	Norwegian Nursing Association
Cost/h MI calls	Per patient	31.9×3.3 (ML)×1.4		Norwegian Nursing Association
Telephone cost/h	Per patient		2.16	Telenor Group
Total cost of MI intervention ²	Per patient		243	
<i>Primary and secondary care (cost group 1)</i>				
General practitioner	Per visits	Treatment time 20 min	84.6	The Norwegian Directorate of Health/The Norwegian Health Economics Administration (HELFO) and "Normal Tariff for private general practice in 2012"
Telephone consultations	Per talk		10	
Dermatologist	Visit	Reimbursement (DRG)	144	The Norwegian Directorate of Health/HELFO
UVB treatment/after 1 July 2012	Visit	Reimbursement (DRG)	37/72	
Specialists (internist and rheumatologist)	Visit	Reimbursement/charge	180/173	The Norwegian Directorate of Health/HELFO
Physiotherapy	Per treatment	Charge (1 h)	114.5	Norwegian Physiotherapy Association (NFF)
Manual therapy	Per treatment	Charge (1 h)	163	NFF
Chiropractor	Per treatment*	Charge	88/54	The Norwegian Directorate of Health/HELFO
Psychologist	Per treatment	Treatment time: 1 h	187	The Norwegian Directorate of Health/HELFO
Hospital stay caused by psoriasis	Days	Reimbursement (DRG)	3539	HELFO
Cost of alternative treatment ³	Visits	Estimated	80–174	Checked 10 different tenderer and estimated a mean charge
Travel costs	Per visit	Estimated 2.5 visits/year	21	The Norwegian Directorate of Health (SAMDATA 2012)
<i>Psoriasis medication, OTC and self-care products, (cost group 2)</i>				
Cost of OTC medication	Various			Local pharmacy/The Norwegian Pharmaceutical Product Compendium
Patient-administered biological medicines ⁴	Various dependent on drug	DRG5 1 month/3 months	16,230.5/48,690	The Norwegian Directorate of Health/HELFO and The Norwegian Pharmaceutical Product Compendium
Methotrexate	Tablets per week		0.3 (1 tbl)	The Norwegian Pharmaceutical Product Compendium
<i>Production loss (sick leave), (cost group 3)</i>				
Median wage in Norway 2012	Hours	Wage rate per day	371.43	SSB: Statistics Norway

¹Euro=7.47 NOK, ²Estimate based on the minimum wages as of 6 June 2012, from the Norwegian Nurses' Association, for a registered nurse with 10 years' experience (1 h work=€31.87) *1.4 (social expenditures). Cost of MI intervention: 1.4=gross wage *1.4 social expenditures, ML: mean length of the MI interv: 3.3 h. ³Healer, podiatrist, acupuncturist, homeopath ⁴Etanercept (Enbrel), adalimumab (Humira) and golimumab (Simponi); *Different costs visit 1 and visits 2–14.

OTC: over-the-counter; DRG: Diagnosis-Related Group; tbl: tablet; MI: motivational interviewing.

Table SIII. Cost of the motivational interviewing (MI) intervention, healthcare services and psoriasis treatment and productivity loss

Cost (€)	Study group (€)				Control group (€)				Between-group difference after the intervention (T3 + T4 (confidence interval), <i>p</i> -value
	Mean (SD)				Mean (SD)				
	T1	T3	T4	T4	T1	T3	T4	T4	
<i>Total cost: MI intervention</i>									
General practitioner (consult + telephone)	0	243 (65)	0	0	0	0	0	0	243 (227,254), <i>p</i> < 0.001
Dermatologist	186 (158)	152 (167)	120 (115)	101 (131)	231 (465)	130 (137)	101 (131)	101 (131)	44 (-47, 136), <i>p</i> = 0.34
UVB treatment	113 (142)	47.5 (97)	33 (73)	73 (131)	248 (962)	100 (194)	73 (131)	73 (131)	-105 (-189,-20), <i>p</i> = 0.016
Hospital admittance due to psoriasis	83 (216)	33 (144)	21 (164)	83.5 (201)	119 (382)	59 (241)	83.5 (201)	83.5 (201)	-104 (-216, 8), <i>p</i> = 0.068
Allied healthcare ¹	977 (8,389)	0 (0)	55 (443)	0.00 (0.0)	830 (6,881)	106 (851)	0.00 (0.0)	0.00 (0.0)	-61 (-320,199), <i>p</i> = 0.65
Other medical specialists ²	307(601)	158 (382)	215 (474)	232 (626)	276 (731)	130 (501)	232 (626)	232 (626)	-4 (-338,330), <i>p</i> = 0.98
Alternative health products	37 (95)	32 (80)	20 (67)	32 (127)	69 (357)	49 (205)	32 (127)	32 (127)	-37 (-115, 41), <i>p</i> = 0.35
Alternative treatment ³	14.5 (64)	0.7 (6.3)	0.06 (0.4)	6.8 (33)	47 (189)	6 (24)	6.8 (33)	6.8 (33)	-14 (-24, -3), <i>p</i> = 0.011
Total costs: Cost group 1	22 (71)	37 (189)	30 (107)	59 (157)	57 (186)	90 (260)	59 (157)	59 (157)	-118 (-220,-16), <i>p</i> = 0.002
Prescription anti-PSO topical treatment (without hydrocortisone (HK))	1,746 (8,473)	464 (634)	526 (766)	579 (806)	1,876 (7,904)	674 (1,512)	579 (806)	579 (806)	-351 (-970, 268), <i>p</i> = 0.27
Prescription topical medication with HK	49 (84)	58 (94)	63 (86)	83 (144)	51 (66)	80 (92)	83 (144)	83 (144)	-37 (-98, 23), <i>p</i> = 0.22
Systemic psoriasis treatment	13 (24)	41 (74)	32 (54)	33 (50)	8 (16)	31 (49)	33 (50)	33 (50)	9.8 (-22, 42), <i>p</i> = 0.54
Biological treatment (DRG-based)	11 (38)	18 (56)	14 (55)	21 (71)	17 (66)	15 (69)	21 (71)	21 (71)	-6 (-55, 43), <i>p</i> = 0.81
OTC body lotion and emollients	0 (0)	0 (0)	0 (0)	401 (1,306)	0 (0)	316 (1,170)	401 (1,306)	401 (1,306)	-799(-1499, -101), <i>p</i> = 0.025
Total costs: Cost group 2	90 (102)	114 (88)	119 (107)	102 (192)	87 (135)	113 (150)	102 (192)	102 (192)	8.9 (-92, 110), <i>p</i> = 0.86
Total costs: Cost group 3	185 (169)	228 (167)	232 (163)	657 (1,332)	239 (542)	547 (1,183)	657 (1,332)	657 (1,332)	-806 (-1518, -95), <i>p</i> = 0.027
Total costs: Cost group 3	1,127 (3,133)	1,632 (4,318)	1,382 (3,795)	1,952 (4,652)	1,986 (4,824)	2,478 (5,380)	1,952 (4,652)	1,952 (4,652)	-1048 (-3874, 1777), <i>p</i> = 0.46

T1: baseline, T3: 3 months after CHT (after the MI intervention), T4: 6 months after CHT. Cost group 1: Use of primary and secondary healthcare; Cost group 2: (Pso-therapy, syst + topical, OTC and self-care products); Cost group 3: Productivity loss for employed patients. CI: confidence interval, 1 Euro (2012)=7.47 NOK, ¹as physiotherapist, manual therapist, chiropractor, psychologist, ²as rheumatologist, internist + assumed travel expenses, ³as healer, homeopath, podiatrist. Significant values are shown in bold.
SD: standard deviation; DRG: Diagnosis-Related Group; OTC: over-the-counter; CHT: climate heliotherapy; UVB: ultraviolet B; PSO: psoriasis.

Table SIV. Total cost for the different cost groups

Cost groups	Study group (€) Mean (SD)	Control group (€) Mean (SD)	Between-group difference, (CI), €, <i>p</i> -value
*Total cost: Cost group 1 (T3&T4)	940 (1177)	1,291 (2,074)	-351 (-970, 268), <i>p</i> =0.27
*Total cost: Cost group 2 (T3&T4)	464.4 (276)	1,271 (2,544)	-806 (-1518, -95), <i>p</i>=0.027
*Total cost: Cost group 3 (T3&T4)	3,069 (6965)	4,118 (8,656)	-1,048 (-3874, 1,777), <i>p</i> =0.46
Total cost: MI (T3)	241(65)	0 (0)	241 (227, 254), <i>p</i><0.001
*Summarized ALL cost groups +MI (T3&T4)	4,212 (5931)	5,992 (7,948)	-1,780 (-4,567, 1,035), <i>p</i> =0.21
*Summarized cost group 1&2 and MI	1,606 (1281)	2,708 (3,928)	-1,103 (-2,293, 87,11), <i>p</i>=0.058

*Costs here are not included cost at baseline=cost for the 3 months prior to the intervention, T3: 3 months after CHT (after the MI intervention), T4: 6 months after CHT, Cost group 1: use of primary and secondary healthcare, Cost group 2: hydrocortisone, systemic PSO therapy, topical therapy, OTC and self-care products, Cost group 3: productivity loss for employed patients. Significant values are given in bold.

SD: standard deviation; MI: motivational interviewing; OTC: over-the-counter; CHT: climate heliotherapy; PSO:psoriasis.

Table SV. Consumption volume of topical and emollient therapy

Consumption volume	Baseline		After 3 months		After 6 months		Differential group difference after the intervention (T3 +T4), <i>p</i> -value
	Mean g (SD)	Median (min–max)	Mean g (SD)	Median (min–max)	Mean (SD)	Median (min–max)	
	MI (<i>n</i> =86)	TAU (<i>n</i> =83)	MI (<i>n</i> =72)	TAU (<i>n</i> =63)	MI (<i>n</i> =65)	TAU (<i>n</i> =60)	
Total amount of used HC and prescription anti-PSO medicine (all topical treatment)	78 (159) 167.50 (0–1,660.00)	70 (105) 100.00 (0–1,240.00)	67 (108) 120.00 (0–2,120.00)	92 (107) 130.00 (0–1,660.00)	92 (157) 120.00 (0–1,200.00)	95 (164) 125.00 (0–1,225.00)	<i>Z</i> =–0.32, <i>p</i> =0.75 ^a
Total amount of used OTC body lotion and emollients	836 (1,028) 500.00 (0–5,350.00)	812 (1,139) 500.0 (0–7,750.00)	1,169 (977) 1,000.00 (0–4,960)	1,032 (966) 925.00 (0–5,500.00)	1,235 (1,207) 1,000 (0–6,175.00)	971 (1,522) 600.00 (0–10,380.00)	<i>Z</i> =–1.44, <i>p</i> =0.15 ^a

T3: 3 months after CHT (after the MI intervention); T4: 6 months after CHT. Cost group 2: use of self-care products (hydrocortisone (HK), systemic psoriasis therapy, topical treatment, emollients and body lotion) at each follow-up, by treatment group (mean, SD) or (mean, SD and median (min–max)).
^aMann–Whitney U test of medians.

PSO: psoriasis; HC: healthy controls; TAU: treatment-as-usual; CHT: climate heliotherapy; SD: standard deviation; MI: motivational interviewing; OTC: over-the-counter.